MALE AGEING AND BONE MINERAL DENSITY IN A SAMPLE OF PORTUGUESE MEN

Raquel Lucas,* Cláudia Silva,* Lúcia Costa,** Domingos Araújo,**,*** Henrique Barros*

Abstract

Aim: In this study we aimed to estimate the prevalence of osteoporosis and to identify the factors associated with bone mineral density in Portuguese men and to quantify age-related bone loss.
Participants and methods: We designed a cross-sectional evaluation of 739 apparently healthy men (20-82 years) recruited during general practice routine visits who volunteered for bone mineral density measurement. Men reporting secondary causes for osteoporosis or using medication known to interfere with bone metabolism were excluded (n=82). Distal forearm bone mineral density was measured using single X-ray absorptiometry (DTX 100, Hologic) and information on demographic, anthropometric, and behavioural aspects was recorded.
Results: Forearm bone mineral density decreased significantly with age (r=-0.29, p<0.001) and was higher in overweight men, and among those who reported moderate or intense physical activity. The prevalence of osteoporosis increased from 1.9% at 40-49 years to 18.6% after 70 years (p<0.001). Increasing age was a risk factor and body mass index was protective against the condition.
Conclusion: This study showed that bone loss is an important problem in ageing men in our country.

Keywords: Age; Bone Mineral Density; Men; Osteoporosis; Portugal

Resumo

Objectivos: Este trabalho teve como objectivos estimar a prevalência e identificar os factores associados à osteoporose numa amostra de homens portugueses e quantificar a perda de massa óssea relacionada com a idade.
Métodos: Foi desenhada uma avaliação transversal de 739 homens aparentemente saudáveis (âmbito de idades: 20 - 82 anos) recrutados em Centros de Saúde portugueses e que voluntariamente procuraram realizar uma medição da densidade mineral óssea. Foram excluídos os 82 indivíduos que referiram causas de osteoporose secundária, bem como os medicados com fármacos que interferem no metabolismo ósseo. A densidade mineral óssea no antebraço distal foi medida por absorciometria radiológica mono-fotónica (DTX 100, Hologic) e foi registada informação demográfica, antropométrica, comportamental e clínica.
Resultados: A densidade mineral óssea no antebraço diminuiu significativamente com o aumento da idade (r=-0,29; p<0,001) e foi mais elevada nos homens com excesso de peso e nos que referiram actividade física moderada ou intensa. A prevalência de osteoporose aumentou de 1,9% na classe etária dos 40 aos 49 anos para 18,6% a partir dos 70 anos (p<0,001). A idade avançada foi factor de risco e o excesso de peso factor protector na osteoporose.
Conclusão: O presente estudo indicou que a perda de massa óssea é um problema importante associado ao envelhecimento da população masculina em Portugal.

Palavras-chave: Densidade Mineral Óssea; Homens; Osteoporose; Portugal

Abbreviations

BMD – Bone mineral density
BMI – Body mass index
OR (95%CI) – Odds ratio (95% confidence interval)

Introduction

Female bone loss, osteoporosis and bone fractures

*Serviço de Higiene e Epidemiologia, Faculdade de Medicina da Universidade do Porto, Porto, Portugal
**Serviço de Reumatologia, Centro Hospitalar do Alto Minho, Ponte de Lima, Portugal
***Associação Portuguesa de Osteoporose

Source of funding: Laboratórios Sanofi-Aventis

are recognised as major public health problems in the ageing population in Western societies.[1] Though hip fractures in men account for one third of all hip fractures and have a higher case fatality rate than in women,[2] male osteoporosis has been a relatively neglected disorder and a clear case definition is still not consensual.[1] Over the last decade, the number of studies examining the incidence of fractures, the distribution of bone mineral density or lifestyle risk factors associated with bone loss in men has increased.[3-6] Recently, the international MrOS study indicated that tricyclic antidepressant use, history of fracture at or after age 50, inability to complete a narrow walk trial, falls in previous year, age ≥80 years, depressed mood, and decreased total hip BMD were independent predictors of non-spine fractures in men over 65 years old.[7] The same study disclosed hormonal pathways in bone loss mechanisms, supporting the hypothesis that the association between weight loss and bone loss at the hip in older men is magnified by sex steroid insufficiency, namely low baseline estradiol, higher baseline sex hormone-binding globulin and greater decline in testosterone.[8]

The process of age-related bone loss is also a subject of current interest. A recent study of the longitudinal changes in bone mass in elderly men indicated that forearm areal bone mineral density was determined by the net loss in bone mineral content that occurs with advancing age. Forearm bone loss was determined by endosteal bone loss, rather than periosteal apposition, which remained constant.[9]

At a populational level, however, there is a relative lack of comprehensive information on the distribution of bone mineral density and on the determinants of male osteoporosis, compared to the worldwide extensive data available on women. Additionally, and probably as a consequence of that, a recent study on osteoporosis treatment in men suggested that there is under-ascertainment and under-treatment of osteoporosis and modifiable secondary causes in older men with fractures.[10]

Therefore, the purpose of this study was to estimate the prevalence of osteoporosis in the forearm and to identify the factors associated with bone mineral density in Portuguese men.

Participants and Methods

A cross-sectional study was conducted in a non-random sample of male volunteers, recruited during general practice routine visits in different regions of Portugal. Eligible participants were all men who voluntarily approached the research team at the primary care centre in order to undergo bone densitometry. Evaluations were equally distributed throughout one calendar year. The research team provided an explanation about the objectives and methods of the planned assessment and invited volunteers to undergo a forearm bone mineral density measurement and a short questionnaire. In the present study we used data from 821 Caucasian community-dwelling men (age 20-99 years), who accepted to participate in the study by giving oral informed consent. Participants were not selected according to their health status, and no information was systematically collected on osteoporosis or fragility fracture history. However, those presenting chronic metabolic or degenerative diseases (such as cancer, type 1 diabetes or renal failure), or using drugs that are known to influence bone metabolism (glucocorticoids, diuretics) were excluded from the present analysis. According to these criteria we excluded 82 subjects. We used data from the remaining 739 apparently healthy men aged 20-82 years. No information on non-participants was collected.

Bone mineral density (BMD) was measured in the non-dominant distal forearm, using one-third radius as region of interest, by single X-ray absorptiometry (Hologic DTX 100). Daily calibration of the densitometer, subject positioning, soft tissue correction and routine analysis were conducted using a standard protocol. The coefficient of variation for repeated measurements of a standard phantom and for repeated measurements of the forearm was 1%.

All participants answered a brief questionnaire applied by trained professionals, comprising information on demographic, behavioural and clinical characteristics. We recorded age, weight, and height as self-reported by participants. Body mass index (BMI) was calculated as weight (kg) / height (m^2) and categorised according to the World Health Organization classes: normal (<25.0 kg/m^2), overweight (25.0-29.9 kg/m^2) and obese (>29.9 kg/m^2). Additionally, present smoking habits and daily intake of alcoholic beverages (only wine and beer were considered) were inquired. Consumption of dairy products was evaluated in large categories, aiming at ordering individuals in three levels of intake (none, equivalent to less than or equal to 500 ml and equivalent to over 500 ml of milk per day) rather than quantifying precise amounts of calcium. The cut-off used was 500 ml of milk in order to facilitate interpretation and conversion to other dairy products amounts. No information was collected on the use of calcium or vitamin D supplementation. Work physical activity was described by participants and classified by the research team in sedentary or non-sedentary and leisure-time activity was grouped as low, moderate or intense. As was the case for dairy consumption, three global broad categories were created by collapsing these two variables: sedentary – light home or occupational activity and no leisure time exercise; moderate activity – either non-sedentary occupation or regular exercise; intense physical activity--non-sedentary work and regular exercise. No information on socioeconomic status or level of formal education was collected.

The International Society for Clinical Densitometry proposes the use of a uniform Caucasian male normative database for men.[11] In order to calculate these reference values we used bone mineral density measurements for male participants of this study aged 20 to 39 years. Osteoporosis was defined as bone mineral density over 2.5 standard deviations below the young male reference mean, according to the cut-off value proposed by the World Health Organization for women.[12]

Results are presented as mean (95% confidence intervals) or as point prevalence, in percentage. The association between continuous variables was assessed using Pearson's correlation coefficient. Mean values were compared using Student's t test or analysis of covariance, as appropriate. In order to evaluate risk factors for osteoporosis data were analysed in a case-control approach. Only participants with 40 years and older were considered for this purpose, once younger individuals were used as reference and thus the prevalence of osteoporosis would be, by definition, almost nil. The magnitude of the associations was quantified by estimating crude and adjusted odds ratios using unconditional logistic regression and corresponding 95% confidence intervals (Stata, version 9.0).

Results

In our sample, as shown in Table I, crude mean BMD (95% confidence interval) decreased from 0.556 (0.546-0.566) g/cm^2 in the 20-39 year-old group to 0.490 (0.474-0.506) g/cm^2 for those aged 70 years or more, p<0.001. There was a significant inverse linear correlation between age and forearm bone mineral density (r=-0.29, p<0.001, Figure 1). Additionally, obese men had higher forearm BMD [0.536 (95%CI: 0.525-0.547) g/cm^2] than overweight [0.539 (95%CI: 0.534-0.544) g/cm^2] and normoponderal participants [0.525 (95%CI: 0.518-0.532) g/cm^2], p=0.016. Participants reporting more intense physical activity also had slightly higher mean BMD values [0.543 (95%CI: 0.534-0.552) g/cm^2] than those reporting moderate physical activity [0.542 g/cm^2 (95%CI: 0.536-0.548] and both had significantly higher BMD values than sedentary participants [0.521 g/cm^2 (95%CI: 0.515--0.527], p<0.001. These differences remained significant after adjusting for age, BMI or both, as appropriate (Table I). We found no significant differences in crude or adjusted mean BMD according to present intake of alcoholic beverages, consumption of dairy products or smoking habits.

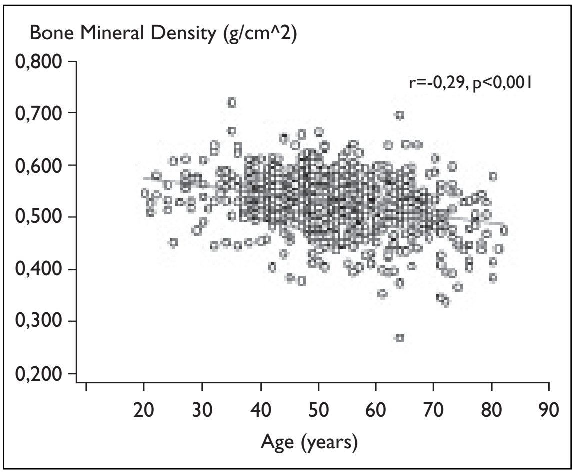

Figure 1. Age and distal forearm bone mineral density in Portuguese healthy men

The overall prevalence of osteoporosis in subjects aged over 39 was 4.3% and increased from 1.9% at 40-49 years to 18.6% after 70 years (p<0.001). The odds of osteoporosis increased significantly with age, mainly after 60 years-old [($OR_{50\text{-}59}$ (95%CI): 1.48 (0.43-5.14)], $OR_{60\text{-}69}$ (95%CI): 4.20 (1.29-13.68), $OR_{>69}$ (95%CI): 11.74 (3.58--38.48). On the contrary, the condition was less frequent in overweight participants [($OR_{overweight}$ (95%CI): 0.32 (0.14-0.72)], but not clearly so in obese men (OR_{obese} (95%CI): 0.38 (0.11-1.30)). These associations remained significant after adjustment

Table I. Crude and adjusted mean (95% confidence intervals) distal forearm bone mineral density (BMD, g/cm²) in healthy Portuguese men.

	n	Crude mean BMD	95% CI	Adjusted mean BMD*	95% CI
Age (years)					
20-39	90	0.556	0.546-0.566	0.558	0.547-0.569
40-49	209	0.544	0.537-0.550	0.545	0.537-0.552
50-59	249	0.534	0.528-0.540	0.534	0.527-0.541
60-69	132	0.519	0.509-0.529	0.520	0.511-0.529
≥70	59	0.490	0.474-0.506	0.491	0.477-0.504
P		<0.001		<0.001	
BMI (kg/m²)					
≤24.9	281	0.525	0.518-0.532	0.520	0.514-0.526
25.0-29.9	363	0.539	0.534-0.544	0.534	0.528-0.540
>30.0	95	0.536	0.525-0.547	0.535	0.524-0.546
P		0.016		0.010	
Smoking					
No	389	0.532	0.527-0.537	0.529	0.523-0.535
≤20 cig/day	133	0.540	0.530-0.550	0.532	0.522-0.542
>20 cig/day	82	0.542	0.530-0.553	0.533	0.521-0.545
Ex-smoker	135	0.525	0.515-0.535	0.527	0.518-0.536
P		0.091		0.770	
Alcoholic beverages (ml/day)					
0	205	0.528	0.520-0.536	0.526	0.518-0.534
<500	425	0.536	0.531-0.541	0.532	0.526-0.538
500-1000	99	0.534	0.523-0.545	0.530	0.519-0.541
>1000	10	0.503	0.456-0.549	0.511	0.474-0.548
P		0.362		0.346	
Dairy products (measured as ml of milk per day)					
0	158	0.528	0.520-0.536	0.527	0.518-0.536
≤500	500	0.534	0.529-0.539	0.529	0.523-0.535
>500	81	0.539	0.525-0.553	0.536	0.524-0.548
P		0.264		0.478	
Physical Activity					
sedentary	322	0.521	0.515-0.527	0.523	0.517-0.529
moderate	264	0.542	0.536-0.548	0.537	0.530-0.544
Intense	153	0.543	0.534-0.552	0.535	0.526-0.544
P		<0.001		0.003	

*Adjusted for age, BMI and physical activity, as appropriate, using analysis of covariance
CI – confidence interval

for all covariates (present intake of alcoholic beverages, consumption of dairy products, smoking habits, and physical activity). Alcohol consumption and dairy products intake were not associated with osteoporosis. The significance of the association of physical activity with bone mineral density was lost when considering osteoporosis as the outcome (Table II).

Discussion

In the present investigation, using a convenience sample of healthy Portuguese men, we found that bone mineral density decreased with advancing age, and we observed a significant protective effect of body mass index and physical activity. The 4.3% prevalence of male forearm osteoporosis was simi-

Table II. Factors associated with osteoporosis in Portuguese healthy males.

	n (%)*	OR (95% CI)	Adjusted OR (95% CI)**
Age (years)			
40-49	209 (1.9)	1***	1***
50-59	249 (2.8)	1.48 (0.43-5.14)	1.58 (0.45-5.60)
60-69	132 (7.6)	4.20 (1.29-13.68)	3.99 (1.14-13.94)
≥70	59 (18.6)	11.74 (3.58-38.48)	11.79 (3.17-43.81)
BMI (kg/m^2)			
≤24.9	241 (8.3)	1***	1***
25.0-29.9	318 (2.8)	0.32 (0.14-0.72)	0.32 (0.14-0.74)
≥30.0	90 (3.3)	0.38 (0.11-1.30)	0.29 (0.08-1.14)
Smoking			
No	347 (3.7)	1***	1***
Ex-smoker	110 (4.5)	2.42 (1.05-5.54)	1.54 (0.48-4.91)
≤20 cigarettes/day	64 (4.7)	1.22 (0.43-3.51)	1.62 (0.41-6.46)
>20 cigarettes/day	128 (8.6)	1.26 (0.35-4.57)	2.28 (0.93-5.63)
Alcoholic beverages (ml/day)			
0	171 (8.2)	1***	1***
<500	374 (2.9)	0.36 (0.15-0.76)	0.39 (0.16-0.92)
500-1000	95 (5.3)	0.62 (0.22-1.79)	1.96 (0.30-12.74)
>1000	9 (22.2)	3.20 (0.61-16.9)	
Dairy products (measured as ml of milk per day)			
0	148 (6.1)	1***	1***
≤500	437 (4.3)	0.70 (0.31-1.59)	1.01 (0.41-2.50)
>500	64 (6.3)	1.03 (0.30-3.47)	0.97 (0.26-3.66)
Physical Activity			
sedentary	288 (6.6)	1***	1***
moderate	236 (3.4)	0.50 (0.21-1.16)	0.84 (0.33-2.11)
intense	125 (4.0)	0.59 (0.22-1.62)	1.21 (0.38-3.79)

*Number of participants and proportion with osteoporosis (T-score≤-2.5), using as reference population men aged 20 to 39 years-old in the present sample
**Odds Ratio (OR) and 95% confidence intervals (CI), adjusted for all variables present in the table, using unconditional logistic regression
***Reference class

lar to the 3-6% estimate after the third National Health and Nutrition Examination Survey, in the United States,[13] and to the 4.8% prevalence found in a Canadian population,[14] both also based on male cut-offs.

However, when considering recent estimates of forearm osteoporosis, the prevalence among Portuguese men was lower than the 13.6% estimate in the MINOS cohort[15] and than the 8.1% prevalence found in Spain.[16] Although the observed disparity between these two geographically close populations may reflect true differences, the non-probabilistic sampling method used in the present study limits our external validity. It is likely that our study is affected by some degree of selection bias, since the studied sample was composed of men who were recruited during their visits to the general practitioner. These participants probably differ systematically from those we would not be able to reach using this sampling method, namely regarding socioeconomic characteristics.[17] Additionally, we did not collect information on non-participation, not allowing for an estimation of the magnitude of a predictable selection bias. Therefore, our study design impairs a possible extrapolation to the Portuguese general male population, limiting the possibility of inference regarding the populational burden of disease. An additional methodological constraint of this study, which presents inherent additional validity and precision limitations, is the choice of self-reported information (height, weight) and concise instruments (dairy products consumption, physical activity) in order to classify individuals according to the covariates levels.

Osteoporosis is less common in men than in women and has been associated with biomarkers, drugs and behaviours that interfere with bone mass such as serum estradiol, high-dose glucocorticoids, excessive alcohol intake or smoking.[8,18-21] However, as shown in this study, low bone density is also an important problem in men in the absence of such medical situations.

It is unknown how far the decline in BMD is an inevitable part of the ageing process and how great the potential is for prevention. There are problems in drawing conclusions about changes in bone density or its relation with different exposures from cross-sectional data, mainly because period and cohort effects are difficult to separate from age influence. In our sample, as found by others, there was a significant age-associated decrease in mean BMD and a marked increased in the risk of osteoporosis, independently of BMI or physical activity. The age-related declines in male testosterone, androgens, growth hormone, and insulin-like growth factor 1 may lead to reduced bone formation and to bone loss[22] and contribute to explain this finding. A longitudinal study of bone loss at the forearm in French men in a similar age range indicated a higher correlation value of -0.40 compared to -0.29 in the present study.[15] However, this association is not generalizable to other anatomical sites: in the MrOS study each 5-year increase in age was associated with 2.6% lower femoral neck BMD, but 7% higher spine BMD, a difference which was attenuated by adjustment to body weight.[23]

Body mass index and self-reported physical activity also presented an effect on BMD independent of age and it is possible to conclude that measures leading to modifications in lifestyle factors might at least partly prevent the age effect. The relation between BMI and bone density deserves a special interest because the adverse effects of overweight, namely on cardiovascular mortality, need to be balanced with the cross-sectional protective effect that obesity seems to present against osteoporosis, both in men and women.[24] Recently a specific effect of weight on hip bone mineral density has been found in MrOS: an increase of 11.5 kg was associated with 3% greater age-adjusted femoral neck BMD but no such association was found for lumbar spine.[23]

Though we found an increase in BMD with level of exercise, no dose-effect relation was present, and there was no significant effect of physical activity on osteoporosis (men who reported intense physical activity presented a slightly increased risk after adjustment for confounders). These different results can merely reflect the fact that, from a statistical point of view, continuous variables may provide more information but may be explained by misclassification error, as physical activity was assessed just according to type of job and leisure time activities, regardless of the duration and the frequency of exercise. The differences between our extreme classes cannot be regarded as representing extremes of exercise but only the normal range of activity likely to be found in daily living. Moreover, the effect of physical activity on bone dynamics has been considered difficult to assess,[25] and a previous cross-sectional study showed no impact of recreational activity on bone mineral density in middle-aged men.[26] Although vigorous physical activity has been shown to decrease the risk of hip fracture[27], the European Prospective Osteoporosis Study found no association between the occurrence of vertebral fractures and either current daily activity, or lifelong physical activity undertaken at work and home.[5] Nevertheless, and possibly more relevant than the prevention bone loss, the role of exercise in decreasing fracture risk may be attributable to improvements in muscular strength and coordination.[28] This hypothesis has been confirmed in the United States, where velocity in accomplishing a physical assignment, balance, and grip strength were associated with BMD.[23]

The role of other lifestyle factors in bone loss and in the risk of osteoporosis remains also unclear. Previous investigations showed conflicting results regarding the effect of milk consumption in preventing osteoporosis. Calcium consumption through food seems to have a modest effect on male bone mineral density at the hip but not at the spine and calcium supplementation may have no effect at all.[23] A recent meta-analysis of prospective cohort studies showed that self-reported low milk intake was not associated with increased fracture risk, both in men and women.[29] As was the case with our questionnaire, most studies assess short-term milk consumption or calcium intake and relate it to present BMD, mainly to avoid recall bias. The effect of diet on bone metabolism is different according to age and especially important during peak bone mass attainment,[30] and knowledge about distant past consumption would provide different clues for understanding the process of osteoporosis.

The effect of chronic alcohol consumption on bone mass in the absence of liver disease is not clear. We found no significant differences in mean BMD or osteoporosis prevalence according to present intake of alcoholic beverages. However, a non-significant lower BMD and an expected higher risk of osteoporosis were found for heavy drinkers but the number of exposed subjects was too small to infer any real adverse effect. A pooled analysis of data from three large cohort studies confirmed that high alcohol intakes conferred a significantly increased fracture risk, independently of bone mineral density. Additionally, the same study suggested a threshold effect of two units of alcohol per day, above which risk significantly increased.[31] Other studies have suggested an apparent protective effect of moderate alcohol intakes, probably because abstainers may have higher risk than light drinkers.[23,32]

Cigarette smoking has been shown to modestly increase the risk of fracture in both sexes[33] but has also shown no effect in hip or spine bone mineral density.[23] In males, we also observed that never smokers presented the lowest prevalence of osteoporosis but ex-smokers presented the highest risk of disease, independently of the effect of age, BMI, physical activity, milk or ethanol consumption. Among ever smokers we found no significant differences between age of beginning of the behaviour (data not shown) but no information is available regarding the number of cigarettes smoked by ex-smokers. It is difficult to explain why ex-smokers presented the highest risk of osteoporosis but a cohort effect cannot be ruled out. Male smoking prevalence is decreasing in our society[34] and marked social and sanitary changes have taken place, making it possible to speculate that these men were more adversely exposed in the susceptible period of peak bone mass attainment.

The usefulness of a young male reference population in the calculation of male T-scores is not consensual. In fact, female cut-offs may be of greater value when the aim is to predict fracture risk in both genders, since they reflect a more conservative estimate. In the present study, we intended to investigate the association between anthropometric and behavioural characteristics and bone mineral density in men, essentially using an aetiological approach, rather than the prediction of fracture risk. Morbidity, mortality, and the associated costs of osteoporotic fractures are well recognised in women, but not as well documented in men. As observed in women, this study showed that age and body mass index were independently associated with bone mineral density and osteoporosis in men and play a significant role in the occurrence of osteoporosis in the Portuguese male healthy population.

Correspondência para
Raquel Lucas
Serviço de Higiene e Epidemiologia
Faculdade de Medicina do Porto
4200-319 Porto – Portugal
E-mail: rlucas@med.up.pt

References

1. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA 2001;285: 785-95.
2. Seeman E. Unresolved issues in osteoporosis in men. Rev Endocr Metab Disord 2001;2:45-64.
3. Kaptoge S, Reid DM, Scheidt-Nave C et al. Geographic and other determinants of BMD change in European men and women at the hip and spine. A population-based study from the Network in Europe for Male Osteoporosis (NEMO). Bone 2007;40:662-673.
4. Lau EM, Leung PC, Kwok T et al. The determinants of bone mineral density in Chinese men—results from Mr. Os (Hong Kong), the first cohort study on osteoporosis in Asian men. Osteoporos Int 2006;17:297--303.
5. Roy DK, O'Neill TW, Finn JD et al. Determinants of incident vertebral fracture in men and women: results from the European Prospective Osteoporosis Study (EPOS). Osteoporos Int 2003;14:19-26.
6. Tracy JK, Meyer WA, Grigoryan M et al. Racial differences in the prevalence of vertebral fractures in older men: the Baltimore Men's Osteoporosis Study. Osteoporos Int 2006;17:99-104.
7. Lewis CE, Ewing SK, Taylor BC et al. Predictors of non-spine fracture in elderly men: the MrOS study. J Bone Miner Res 2007;22:211-219.
8. Ensrud KE, Lewis CE, Lambert LC et al. Endogenous sex steroids, weight change and rates of hip bone loss in older men: the MrOS study. Osteoporos Int. 2006;17:1329-1336.
9. Szulc P, Delmas PD. Bone loss in elderly men: increased endosteal bone loss and stable periosteal apposition. The prospective MINOS study. Osteoporos Int 2007;18:495-503.
10. Feldstein AC, Nichols G, Orwoll E et al. The near absence of osteoporosis treatment in older men with fractures. Osteoporos Int 2005;16:953-962.
11. The International Society for Clinical Densitometry.

2007 Official Positions of the International Society for Clinical Densitometry. URL: http://www.iscd.org/Visitors/pdfs/ISCD2007OfficialPositions-Adult.pdf. accessed on 17th June 2008. 2007.
12. Report of a WHO Study Group. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser 1994;843:1-129.
13. Looker AC, Orwoll ES, Johnston CC et al. Prevalence of low femoral bone density in older U.S. adults from NHANES III. J Bone Miner Res 1997;12:1761-1768.
14. Tenenhouse A, Joseph L, Kreiger N et al. Estimation of the prevalence of low bone density in Canadian women and men using a population-specific DXA reference standard: the Canadian Multicentre Osteoporosis Study (CaMos). Osteoporos Int 2000;11: 897-904.
15. Szulc P, Marchand F, Duboeuf F, Delmas PD. Cross-sectional assessment of age-related bone loss in men: the MINOS study. Bone 2000;26:123-129.
16. Naves M, Diaz-Lopez JB, Gomez C, Rodriguez-Rebollar A, Serrano-Arias M, Cannata-Andia JB. Prevalence of osteoporosis in men and determinants of changes in bone mass in a non-selected Spanish population. Osteoporos Int 2005;16:603-609.
17. Atella V, Brindisi F, Deb P, Rosati FC. Determinants of access to physician services in Italy: a latent class seemingly unrelated probit approach. Health Econ 2004;13:657-668.
18. Amin S, Zhang Y, Sawin CT et al. Association of hypogonadism and estradiol levels with bone mineral density in elderly men from the Framingham study. Ann Intern Med 2000;133:951-963.
19. Hoidrup S, Prescott E, Sorensen TI et al. Tobacco smoking and risk of hip fracture in men and women. Int J Epidemiol 2000;29:253-259.
20. Hoidrup S, Gronbaek M, Gottschau A, Lauritzen JB, Schroll M. Alcohol intake, beverage preference, and risk of hip fracture in men and women. Copenhagen Centre for Prospective Population Studies. Am J Epidemiol 1999;149:993-1001.
21. Van Staa TP, Leufkens HG, Abenhaim L, Zhang B, Cooper C. Use of oral corticosteroids and risk of fractures. J Bone Miner Res 2000;15:993-1000.
22. Khosla S. Role of hormonal changes in the pathogenesis of osteoporosis in men. Calcif Tissue Int 2004; 75:110-113.
23. Cauley JA, Fullman RL, Stone KL et al. Factors associated with the lumbar spine and proximal femur bone mineral density in older men. Osteoporos Int 2005;16:1525-1537.
24. De Laet C, Kanis JA, Oden A et al. Body mass index as a predictor of fracture risk: a meta-analysis. Osteoporos Int 2005;16:1330-1338.
25. Karlsson MK. Skeletal effects of exercise in men. Calcif Tissue Int 2001;69:196-199.
26. Medras M, Slowinska-Lisowska M, Jozkow P. Impact of recreational physical activity on bone mineral density in middle-aged men. Aging Male 2005;8:162--165.
27. Kujala UM, Kaprio J, Kannus P, Sarna S, Koskenvuo M. Physical activity and osteoporotic hip fracture risk in men. Arch Intern Med 2000;160:705-708.
28. Olszynski WP, Shawn Davison K, Adachi JD et al. Osteoporosis in men: epidemiology, diagnosis, prevention, and treatment. Clin Ther 2004;26:15-28.
29. Kanis JA, Johansson H, Oden A et al. A meta-analysis of milk intake and fracture risk: low utility for case finding. Osteoporos Int 2005;16:799-804.
30. Bachrach LK. Acquisition of optimal bone mass in childhood and adolescence. Trends Endocrinol Metab 2001;12:22-28.
31. Kanis JA, Johansson H, Johnell O et al. Alcohol intake as a risk factor for fracture. Osteoporos Int 2005;16: 737-742.
32. Williams FM, Cherkas LF, Spector TD, MacGregor AJ. The effect of moderate alcohol consumption on bone mineral density: a study of female twins. Ann Rheum Dis 2005;64:309-310.
33. Kanis JA, Johnell O, Oden A et al. Smoking and fracture risk: a meta-analysis. Osteoporos Int 2005;16:155--162.
34. Azevedo A, Machado AP, Barros H. Tobacco smoking among Portuguese high-school students. Bull World Health Organ 1999;77:509-514.